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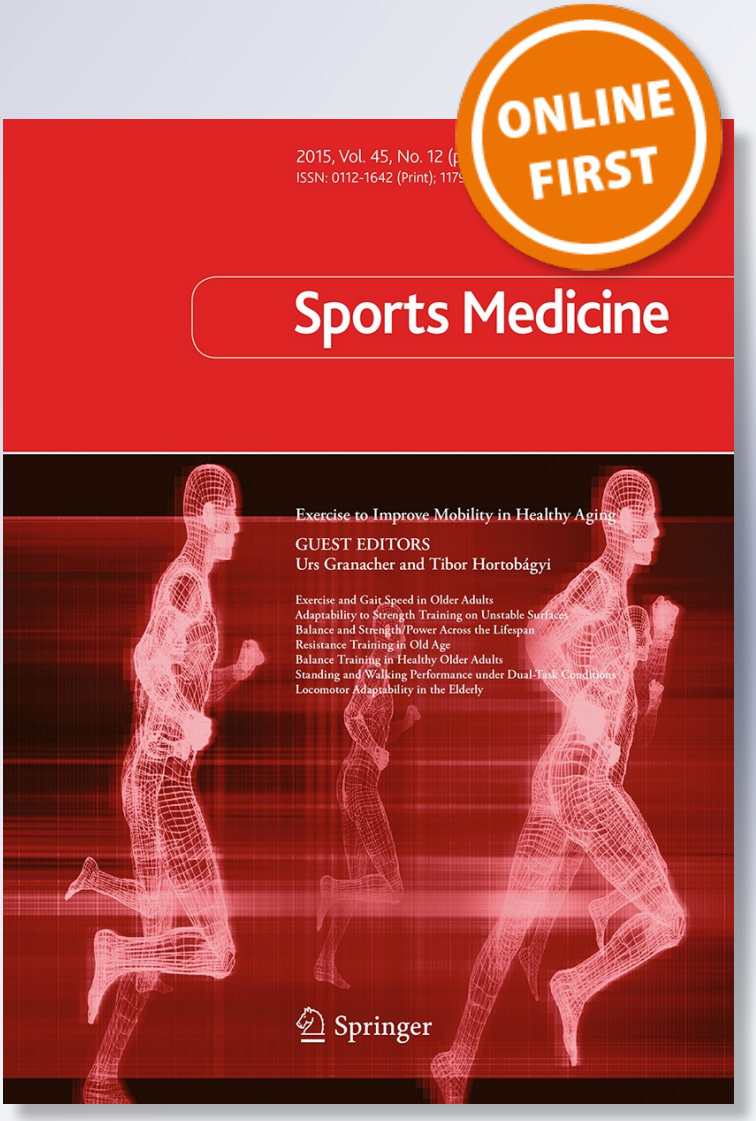

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REVIEW ARTICLE

Can Exercise Positively Influence the Intervertebral Disc?

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Abstract To better understand what kinds of sports and exercise could be beneficial for the intervertebral disc (IVD), we performed a review to synthesise the literature on IVD adaptation with loading and exercise. The state of the literature did not permit a systematic review; therefore, we performed a narrative review. The majority of the available data come from cell or whole-disc loading models and animal exercise models. However, some studies have examined the impact of specific sports on IVD degeneration in humans and acute exercise on disc size. Based on the data available in the literature, loading types that are likely beneficial to the IVD are dynamic, axial, at slow to moderate movement speeds, and of a magnitude experienced in walking and jogging. Static loading, torsional loading, flexion with compression, rapid loading, high-impact loading and explosive tasks are likely detrimental for the IVD. Reduced physical activity and disuse appear to be detrimental for the IVD. We also consider the impact of genetics and the likelihood of a 'critical period' for the effect of exercise in IVD development. The current review summarises the literature to increase awareness amongst exercise, rehabilitation and ergonomic professionals regarding IVD health and provides recommendations on future directions in research.

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Key Points

We examined the literature on the intervertebral disc in sport, exercise, mechanical loading and disuse to understand what kinds of loading protocols could result in positive adaptations of the intervertebral disc.

The synthesis of the literature suggests that dynamic, axial loading of the spine at slow to moderate movement speeds is likely to result in positive adaptations (anabolism) of the disc, whereas high-impact loads, explosive movements, extremes of movement as well as sedentary behaviour, disuse and immobilisation are likely detrimental (catabolic).

The literature indicates that running and upright endurance sports are either beneficial or at least not detrimental to the disc, whereas sports including swimming, baseball, weightlifting, rowing and equestrian riding are more likely to lead to disc degeneration.

1 Introduction: Can Loading Affect the Intervertebral Disc (IVD)?

All organ systems in the human body show some kind of response to loading. In exercise and sport sciences, much focus is on the muscular system. This is in part due to understandable biases: muscles are easy to see, they are easy (or easier) to measure, performing invasive measurements is less problematic, and muscles respond quickly to loading protocols.

In the conservative treatment and exercise management of spinal pain, focus is again largely on the muscle system, likely due to the same understandable biases. However, what about the intervertebral discs (IVDs)? The IVDs are well-recognised as sources of pain and much focus in orthopaedic management of spinal conditions is placed upon these structures. However, in the exercise field, if you ask an exercise professional "What can we do to strengthen the intervertebral disc?", vague and speculative answers may be expected as an initial response. In sports and exercise physiology textbooks it is common to find chapters on the impact of exercise on muscle, bone and tendon, but not on the IVD.

The idea that certain types of loading may 'strengthen', or at least alter, the IVD is not new as a publication from 1984 shows [1]. A later work [2] asked the rhetorical question, "Can the strength of disc tissue be increased?". In IVDs removed at surgery in scoliosis patients, the distribution of types I and II collagen in the IVDs corresponded to the scoliosis curve [1]. Hence, it is clear that IVD tissue, like other tissues, does respond to mechanobiological cues.

The aim of this review was to synthesise the literature to attempt to understand the following:

1. What kinds of exercise and loading protocols are beneficial or detrimental for the IVD?;
2. Can we reasonably expect to 'strengthen' a damaged or degenerate IVD?
3. If not, what should be the goal of exercise?
4. What are the gaps in our knowledge on exercise and the IVD?
5. What are the most likely fruitful steps forward in research on exercise and the IVD?

In answering these questions, we examine the literature on IVD nutrition, cell and whole-disc studies, animal models of exercise, human studies of exercise and the IVD (as measured by the surrogate measure of spinal length or body stature), degeneration of the IVD and the impact of sport, and also measurement approaches for human studies of the IVD.

2 Brief Overview of Disc Homeostasis in Health and Disease: What is Disc 'Health'?

A primary function of the IVD is to enable mobility of the spine. Anatomically, the IVD can be divided into the nucleus pulposus and annulus fibrosus. The nucleus pulposus, in its healthy state, is a hydrated, gel-like tissue rich in proteoglycans, which attract and bind water. The proteoglycans are more prevalent in the nucleus than in the annulus fibrosus [3]. The annulus fibrosus, in its healthy state, consists of approximately 15–25 concentric lamellae of obliquely oriented collagen fibres [4] that surround the nucleus pulposus. The orientation of each lamella alternates from one lamella to the next such that it exhibits a cross-hatched structure. Both the annulus fibrosus [5] and nucleus pulposus [6] are anchored into the cartilaginous end-plates. The gelatinous nucleus pulposus is contained within the annulus fibrosus, meaning that when axial compression force is applied to the IVD, the axial load is converted into pressure in the nucleus and restrained by the annulus fibrosus. This enables mobility whilst retaining a degree of stability.

Numerous papers have been written on the healthy IVD and the changes that occur with IVD degeneration (for an in-depth discussion we refer readers to Adams and Roughley [7] and Vergroesen et al. [8]). Briefly, at an adult age, the extracellular matrix of the IVD is maintained by the nuclear chondrocytes. Under the influence of anabolic mechanobiological cues, predominantly hydrostatic pressure, these cells produce proteoglycans and limited amounts of collagen type II. This is what is referred to as a healthy disc. When hydrostatic pressure is reduced, due to damage to the extracellular matrix, cellular degeneration of the matrix (e.g. due to smoking) or prolonged overloading, shear forces in the IVD are increased, and cells stop producing proteoglycans. When this persists, cells become catabolic and start producing collagen type I instead of proteoglycans, remodelling the gel-like nucleus pulposus to a more fibrous tissue—this is what is referred to as a degenerative disc. A degenerated disc loses its ability to stabilise the motion segment; hence, its primary function is lost. Health and degeneration are further defined in Table 1. As such, in this review we considered the positive influence on the IVD towards the 'healthier state' to be the anabolic mechanobiological cues to increase proteoglycan production. Although we consider a negative definition suboptimal, given the state of the literature in humans, in imaging or cadaver studies of human subjects the best possible definition of disc 'health' was the 'absence of disc degeneration' (see Table 1).

3 Focus of the Review and Consideration of Limitations

We focus on the lumbar spine, in particular when examining human studies, in this review. There were limited data in the literature for cervical and thoracic IVDs as these are, in general, much less well-studied in humans. What may apply to the lumbar IVDs may apply to other regions of the spine, but not necessarily. We performed a narrative review of the literature as publications in the field to date do not permit systematic review or meta-analysis. A systematic review largely depends on having a dependent variable or variables consistent across publications to be compared. This is currently not the case in the IVD and exercise literature.

In this review, due to the limited data available, when examining the human studies we chose to extend the focus to IVD degeneration and, in some instances, unusual spinal features or injuries (Table 1). A number of studies have examined the influence of, for example, sport type or occupational activities on spinal pain and other factors. However, IVD degeneration is more related to the IVD tissue itself than, for example, low back pain. This endpoint is also the most commonly studied IVD parameter in human models. Other structures, such as the vertebral endplates which play an important role in the nutrition of the IVD and the zygapophyseal joints, are less well-studied in terms of the impact of loading, but can also be a source of spinal pain.

Table 1 Definition of disc 'health', disc degeneration and wider spine abnormalities

Characteristics of a healthy intervertebral disc	Characteristics of IVD degeneration [7, 93]	Wider IVD and spine abnormalities [36, 38]
Highly-hydrated gel-like nucleus	Reductions in IVD height	Osteophytes
Distinction of nucleus and annulus on T2-weighted MRI	Loss of IVD signal intensity	End-plate abnormalities (such as Schmorl's nodes)
High signal intensity of nucleus	Indistinct or loss of separation between the nucleus pulposus and annulus fibrosus	IVD bulging
No loss of disc height	Uneven structure	IVD herniation
Anabolic cell response	Catabolic cell response	Spondylolisthesis
Proteoglycan and collagen type II production	Collagen type I production	
High intradiscal pressure	Dehydrated fibrous nucleus	
Low shear forces in the nucleus	Low intradiscal pressure	
Limited neutral zone in bending and rotation	High shear forces in the nucleus	
Limited ROM in bending and rotation	Increased neutral zone in bending and rotation	
	Increased ROM in bending and rotation	

In the studies reviewed, the impact of load or sport on the spine was typically defined by the presence of "deviations from the healthy state" of the IVD, vertebral body or spine. Thus, in line with the current literature, IVD 'health' is defined as the absence of IVD degeneration. These were assessed by radiologists on the basis of radiological examinations (MRI, CT, X-rays). In the case of IVD degeneration, this was typically evaluated on T2-weighted MRIs. It should be noted that while there is a relationship between these kinds of changes and pain [89], the relationship is not 1:1, and that the changes can occur without any symptoms being present [90, 91] and also occur as part of normal aging [92]

CT computed tomography, *IVD* intervertebral disc, *MRI* magnetic resonance imaging, *ROM* range of motion

Finally, in examining the literature on specific topics that are relevant, but not central, to the current review, such as in vitro studies of IVD tissue or cells or genetic influences in IVD degeneration, we refer the reader to recent reviews that have covered these topics extensively. However, we do discuss more recent studies in these areas when relevant.

4 How Does Loading Affect the Disc?

4.1 Disc Nutrition and Load

In the adult state, the IVD is largely dependent upon diffusion through the end-plates for nutrient exchange, although the outer annulus is supplied by blood vessels [9]. Small solutes, such as oxygen and lactate, move through the IVD via diffusion, and a 'pumping action' through movement does not appear to play a role in moving small solutes through the IVD [10–12]. However, there appears to be an optimal amount of disc hydration for the uptake of small solutes into the IVD [13–15]: if hydration is too high or too low, the uptake of small solutes into the IVD is impeded. Disc hydration varies directly with the applied load [16]. Furthermore, a magnetic resonance imaging (MRI) study using contrast agent [17] showed that the speed of penetration of small solutes into the IVD is affected by the amount of load the spine experiences. Hence, the extent of the load, as expressed in the extent of the IVD hydration and size, can affect the supply of small solutes through the IVD.

For larger-size molecules, diffusion is limited and it is difficult for them to move through the IVD [18]. A biomechanical modelling study [19] provided results suggesting that a pumping action (i.e. fluid flow/convection) through movement may play a role in the transport of larger nutrients. Overall, these data show that the movement of nutrients into and through the IVD can be affected by the loading patterns applied to the IVD. Nutrient supply will ultimately impact on tissue health.

4.2 Humans, Exercise and Stature

Changes in body stature occur over the course of a sleep–wake cycle, with increases in height after lying for a number of hours. Typically, adult body height varies by approximately 1 % over the course of a normal sleep–wake lying-activity cycle and is attributed to changes in the IVD [20]. In the 1980s and 1990s a series of studies were performed that examined the effect of one session of exercise on body stature. Reductions in body height or spine length were shown after running and jogging [21–24], jumping activities [25, 26], weighted circuit training and lifting weights [27–30]. It is unsurprising, therefore, that MRI studies have shown reductions in IVD size after walking [31, 32] and running [33, 34]. These changes in IVD size are assumed [35] to be the result of movement of water out of the IVD. At the end of exercise, body stature rapidly recovers [29].

What these studies serve to show is that exercise protocols can result in reductions in IVD size and, most likely, water content. Upon ending exercise, fluid should move back into the IVD, potentially facilitating the influx of nutrients into the IVD. A pattern of exercise–rest–exercise might be more beneficial for the nutrition of the IVD. Overall, these findings show that exercise will result in short-term changes in the IVD, but whether or not this will be negative or positive in long-term exercise is an open issue.

4.3 Humans and Sport

Is there evidence that exercise can have a positive effect on the IVD in humans? In our searches of the literature, we did not find any prospective studies that examined the impact of specific exercise protocols in humans on the IVD. However, a number of, almost exclusively cross-sectional, studies have been performed that examined IVD degeneration and/or spinal abnormalities in specific athletic populations. One of the difficulties in using IVD degeneration or spinal abnormalities as outcome measures is that they focus on 'deterioration' rather than 'health'. The outcome measures are decided by X-ray or MRI classification, which is to a certain extent arbitrary and limited by potential errors in subjective interpretation. There is only a loose correlation of radiological variables with clinical symptoms (Table 1). Nonetheless, this body of literature can be used to gain some insight into the impact of exercise and loading on IVD health.

Overall, there are a number of sport types where thoracic and lumbar IVD or spinal damage are more common. This is seen in sports where traumatic spine injury is more frequent, such as gymnastics [36], wrestling [36–38] and American Football [39], and was similarly seen in sports where repetitive loading of the spine in extremes of motion or load occurs, such as gymnastics [36, 38, 40], cricket [41], weightlifting [37, 42] and rowing [43], and also in sports where the spine is subject to high(er) impact loads with sometimes unpredictable landing forces, such as horseback riding in equestrian events [44] and volleyball [45]. Due to the nature of these sports, it is not surprising that the incidence of IVD or spine abnormalities is higher. Hence, they do not deliver evidence per se for what kinds of loading protocols might be better or worse for the IVD.

Swimmers have previously been used as a reference group on the assumption they would show less IVD

degeneration [45, 46]; however, a recent study found the highest IVD degeneration rates in swimmers (and baseball players) as compared to competitors in basketball, kendo, soccer and running or non-athletes [47]. The authors voiced the opinion that the repetitive twisting activities of swimming and baseball constitute the underlying factor for this effect. Another study from this group showed higher rates of IVD degeneration in elite swimmers than in recreational swimmers [48].

The time spent loading the spine in a sport (such as years of participation), level of participation (elite vs. recreational) and hours of participation per week will all influence the response of the spine to a particular type of sport [46, 48]. For example, Hangai et al. [47] excluded people who had performed their chosen sport for less than 5 years. However, studying athletes of certain levels of participation could help to understand when a particular loading pattern stops being beneficial.

Of the sports examined, running sports [42, 47, 49] appear to either be beneficial or at least not detrimental in terms of IVD degeneration. Hangai et al. [47] did not specify what kinds of runners (e.g. sprinters, middle-distance or marathon runners) constituted their pool and attempts to contact the authors were unanswered. In the works by Videman et al. [42, 49], running and cross-country skiing were classified together as "endurance exercise" and not separated out.

Generally, what the studies on IVD degeneration and sport type deliver is to reaffirm that performing non-physiological (e.g. direction of loading, magnitude of loading, position of loading), unpredictable or impact-loading patterns are detrimental to the IVD. Overall, participation in the investigated sport activities was usually negative for IVD health. However, most of the studies considered elite athletes. Could some of the sports be less damaging if performed more moderately? Finally, there was some evidence that upright activities such as running may have a protective effect on the IVD or, at an elite level, at least not be as detrimental to the IVD as other sports at an elite level.

4.4 Occupations and Manoeuvres that Constitute a Risk for the IVD

Is there evidence from different occupational groups as to what types of activity impact IVD health? It appears there is a U-shaped relationship between lifetime physical activity and IVD degeneration: sedentary occupations and heavy occupations can increase the risk of IVD degeneration [50], with the least amount of degenerative changes in people who performed moderate levels of physical activity. There is also some evidence [51] that prolonged disuse (strict bed-rest) can result in a subsequent loss of water signal intensity from the IVD. Excessive and frequent lifting and/or twisting activities [52] can promote the development of IVD degeneration.

Cadaveric studies make it clear that extremes of load result in damage to spinal structures. Specifically, forceful spine flexion combined with compression can cause a rupture of the posterior annulus fibrosus and result in IVD herniation [53, 54]. This is an obvious concern for acute injury in, for example, lifting-type occupations. High-load axial compression of the spine alone is more likely to cause fractures of the end-plate than direct damage to the IVD [53, 55]. However, this could lead to subsequent IVD degeneration [56, 57]. Torsion, or axial rotation, of the IVD may lead to shearing between the lamellae of the annulus and to concentric tears between the lamellae [58], particularly when combined with lateral bending.

Repetitive lower-load protocols, depending on loading type, may also be a concern. For example, repetitive sub-maximal axial compressive loading can cause end-plate damage and, when combined with flexion, IVD herniation at lower loading levels than needed for one-off loading cycles [59, 60].

Overall, these studies tell us that a lifestyle of a moderate amount of physical activity, which minimises high spinal loading levels and avoids certain riskier loading types, is likely to be more conducive to good IVD health.

4.5 Animals and Exercise

Animal studies have been performed that looked at the effect of exercise over a number of weeks or months on the IVD, and a series of animal studies have shown positive effects of exercise on the IVD. One study [61] in adult dogs evaluated different exercise types over 3 months. The most pronounced effects were seen at the thoracolumbar junction (T12 to L2) and overall improved IVD nutrition was shown (as measured, for example, by increased transport of sulphate and increased uptake of glucose, oxygen and glycogen). All forms of exercise had an effect, although there were some differences between them. The important finding of this study was that, although at the time it was thought that short-duration loading does not impact diffusion of small solutes into the IVD [10–12], long-term exercise led to a physiological adaptation in the IVD to improve IVD nutrition. Another research group evaluated 20 km/day of treadmill running for 15 weeks in dogs [62]. The authors found the wet weight and total collagen of the L1/2 IVD to be increased with exercise [62]. Furthermore, 3 weeks of "moderate" treadmill exercise [63] in rats increased the IVD matrix production and cell number with no increase in cell death. Another study by this group [64] evaluated running in rats and performed analyses at 9, 14, 28, 59 and 105 days after the start of exercise protocol. The

authors found that cell numbers were increased in the IVD stem cell niche and the outer annulus on days 14 and 105 of exercise and in the peripheral epiphyseal cartilage region on day 14. These were considered to be positive effects by the authors.

Other studies have shown both positive and negative effects of exercise in animals, depending on the spinal region or parameter examined. In a series of publications [65–67], a Finnish group evaluated the effect of a 55-week treadmill running protocol in dogs. The group found that collagen synthesis was elevated in the nucleus of lumbar IVDs (likely a negative effect) and posterior annulus of thoracic IVDs (likely a positive effect), but decreased in the nucleus of thoracic IVDs [67]. Other studies (considering sulphate and safranin-O incorporation into the IVD) provided evidence of increased proteoglycan content in the lumbar IVDs and in the cervical (C5) IVD of the exercised dogs [65] and of increased proteoglycan synthesis in the cervical (C5) IVD but reduced in the annulus of the thoracic (T6) IVD [66]. It should be noted that in this group of dogs the running distance was progressed to 40 km/day, which may represent overload for some spinal regions and account for some of the mixed findings.

Another study [68] examined the impact of a series of running exercises for 1–5 months in rats. One of the main findings was that although radiological examination found the discs in the exercised rats to be thinner than controls, when the IVDs were removed and allowed to imbibe fluids there was a much greater increase in the height of the IVDs of the exercised rats than the control rats. The smaller disc height upon the IVDs being removed from the animals could be attributed to an increase in compressive muscle forces due to the exercise. The greater "ability to imbibe fluids" may imply there was a greater proteoglycan content in the IVDs of the exercised rats.

Some studies clearly showed a negative impact of exercise and habitual loading patterns on IVD health. A series of studies [69–71] examined the impact of bipedal walking on the IVD in rats. Overall, these loading protocols resulted in IVD degeneration and herniation, indicating that bipedal walking in quadruped animals loaded the spine in a way that exceeded the physiological operating range of the quadruped IVD.

Overall, it is clear from the animal exercise studies that loading and exercise do modulate IVD properties and nutrition in animals. The effect of prolonged exercise can be positive, with loading in a physiological direction (e.g. normal quadruped locomotion/running in quadrupeds, not bipedal), and of specific intensity and duration (e.g. the duration of running in the Finnish studies with dogs may have been excessive and detrimental for some spinal regions) resulting in positive adaptations.

4.6 Cell, Whole-Disc and Animal External Loading Studies

There have been a number of studies on the impact of loading on IVD cells and whole IVDs. These studies often used samples from animals, although human IVD samples were sometimes used. There have also been a number of studies on the impact of external loading on animal IVDs. These kinds of studies can, within some limitations, give us insight into what loading protocols may be beneficial for the IVD.

Recent review articles [72, 73] provide detailed information on the impact of loading in in vitro and external loading models. Rather than repeat this information here, we refer the reader to those review articles and summarise the overall knowledge base from these review articles as follows:

- Static loading of the IVD is not beneficial to it: more cell death is observed, decreased production of matrix components occurs, and increases in catabolic markers are observed along with reductions of anabolic markers in the IVD.
- IVD immobilisation or disuse typically results in losses of glycosaminoglycans in small-animal models.
- Dynamic loading of the IVD can provide a positive response in the IVD. However, the magnitude of the applied load, its frequency and duration play important roles.
- There appears to be a certain 'physiological range' of dynamic axial compressive loads that result in an anabolic response in the IVD. Outside of this range, a catabolic response is typically seen in the IVD or IVD cells. One review [72] put this range at 0.2–0.8 MPa, with a frequency of 0.1–1 Hz and duration of 8 h/day.
- The responses of degenerated IVDs, IVDs from older animals or cells from such IVDs are not the same as those seen when a given load is applied to young and/or healthy IVDs. For example, a smaller increase in proteoglycan production was seen in response to loading in cells from older and/or degenerated IVDs [74].

Overall, this body of literature helps to underscore the point that the IVD does adapt to loading and that this response may 'strengthen' the IVD, but that loading can also have negative (catabolic) effects.

5 What Kinds of Loading Patterns and Activities are Better for the IVD?

Overall, the information from human, animal, cell and whole-disc studies allows us to suggest a type of loading that is 'probably healthier' for the IVD:

- Type of loading: loading must be dynamic. Static loading, immobilisation and disuse are detrimental. High and/or impact loading is likely detrimental.
- Direction of loading: axial loading, to which the IVD is adapted, must be applied. Extreme ranges of motion, torsional activities and flexion with compression are loading types that are likely detrimental.
- Loading frequency and/or speed: 'slower' loading cycles are probably better. A review [72] of cell and whole-disc tissue studies recommended 6–60 cycles/min, but the extent to which this can be directly applied to a person performing exercise is not clear. The sport literature [44, 45] on IVD degeneration suggests that rapid, high-impact and sudden loading types are detrimental for the IVD. Hence, movement speeds at or around 60 cycles/min (i.e. 1 cycle/sec), which would involve a ballistic component, might be detrimental for the IVD.
- Magnitude of loading: a loading range of 0.2–0.8 MPa, generating intradiscal pressures of 0.3–1.2 MPa, was suggested in a recent review [72] as an optimal range. The intra-discal pressures in a variety of tasks have been measured [75] with static standing, walking and jogging typically falling within this range, but with lying, bending forward in standing, lifting a 20 kg load and certain sitting postures (such as slumped sitting in full flexion) falling outside of this range. High-impact activities and explosive tasks likely generate magnitudes of IVD load outside of this healthy range.
- Duration of loading and load patterning: 8 h/day of loading has been suggested to be appropriate in a prior review [72]. The knowledge base is, however, limited for determining what duration of loading or what kind of unloading–loading patterns are better for the IVD. It is possible that a pattern of exercise–rest–exercise throughout the day is more beneficial, rather than a particular duration of loading per se.

It is also important to consider the time of day in loading. Intradiscal pressure will be higher in the morning than in the evening [75], which implies a higher injury risk. Based on the studies on stature, most of this effect should be gone within the first hour of the day. Therefore, some higher load protocols might be better performed later in the day.

This information enables us to hypothesise the likely benefit of different loading protocols. Activities such as walking and jogging will provide loading in the 'probably healthier' ranges of magnitude, speed, direction (axial) and type (dynamic). Short-distance running and sprinting will likely result in loading patterns that exceed the 'probably healthier' range of magnitude. Elite swimming is likely, overall, to be suboptimal for the disc: loading direction will be in torsion and/or extremes of range and speed of loading will be towards the upper end of the 'probably healthier' range. Amateur swimming is likely to be, at the very least, less detrimental to the IVD, but it is unclear whether this kind of activity will be beneficial for the IVD. Desk jobs involving sitting will likely be detrimental for the IVD: loading is typically static and depending on sitting posture, the magnitude of the load may be outside the likely beneficial range.

From a more ergonomic and population health perspective, at the current juncture we can be fairly certain that for IVD health it is better to (a) not sit or lie down for long periods; (b) stand, walk or go jogging; (c) avoid non-physiological movement patterns, such as sports and activities with extreme ranges of motion, and sports and activities with higher spine injury risk; and (d) construct the work environment to encourage the implementation of healthier loading protocols. However, we may need to consider that static standing for prolonged periods might not be ideal.

6 Can We Reasonably Expect to 'Strengthen' a Damaged or Degenerated IVD with Exercise?

Whilst we are sceptical, we cannot negate the idea that some kinds of exercise may help to facilitate IVD repair. Furthermore, it is also worth considering that IVD degeneration implies impaired material properties and mechanical strength. It is clear [74] that an already damaged or degenerate IVD is unlikely to respond to loading in the same way that a healthy IVD does. Therefore, it has to be considered that loading parameters that are healthier for the IVD may change with, for example, different grades of IVD degeneration.

If exercise cannot 'regenerate' a degenerated IVD, what should the goal of exercise be for the IVD? In this case, we suggest that knowledge on beneficial exercise protocols and loading be implemented in more population-wide interventions, such as lifestyle and ergonomic modification to improve population IVD health.

7 Influence of Genetics on Disc Health

A series of studies have highlighted the importance of familial factors in the development of IVD abnormalities, and a recent review article [76] has summarised the literature in the field of IVD degeneration. Overall, the largest proportion of variance in IVD degeneration was explained by "shared familial factors", which include genetics but

also common behaviour and environmental factors in a particular family. There were also a number of genetic variations associated with an increased risk of IVD degeneration. However, studies examining spinal abnormalities and disc degeneration do have some limitations. The risk estimates of the impact of physical activity could have been biased through crude (i.e. interview only) measurements of loading. Also, extreme loading, e.g. due to participation in elite sport, is probably seldom included in the investigated populations of these prior works. Furthermore, the 'disc degeneration' outcome measure is quite an insensitive outcome measure with, for example, only ten of 41 individuals showing a change of one or two disc degeneration grade(s) in 5 years of aging in one study [77]. This will lead to factors with a more subtle influence being washed out in the analysis and more important factors being further overestimated. Nonetheless, it is clear that familial factors (be it genetics or otherwise) play an important role in IVD degeneration.

Interestingly, it appears that genetic variants can affect the response of the IVD to exercise [78]. Furthermore, as we highlight, loading patterns and sporting types do have an impact on the IVD and from an ergonomic perspective, certain behaviours (such as lifting, bending and twisting) do influence spinal injury risk. Overall, it is important to remember that whilst genetic background plays an important role in all aspects of health, it is important for prevention and management to understand what other factors can modulate risk.

8 Aging and the Disc: A Critical Period for Improving Lifetime Disc Health?

On the basis of anatomical studies, in 1969 Coventry [79] expressed the opinion that development of the IVD should be complete shortly before the age of 30 years, with growth plates being fused in the early twenties and subsequent development of the IVD thereafter. Since that time, a series of cadaveric studies have been conducted that enable some inferences about the development of the IVD.

IVD water content, as measured directly [80, 81] or as implied via T2-weighted signal intensity [82], is highest in infancy and decreases as an individual matures. The sodium content of the IVD increases from infancy [80] up until the age of 20–30 years, implying increases in glycosaminoglycan content. In addition, the degree of creep (reduction in IVD height with constant load relative to baseline height) apparent in an IVD is highest in infancy and decreases towards maturity [81]. Embryotic cells decrease markedly in the IVD by the end of the second decade of life [83]. Viscoelastic state [81], disc height [81] and annulus water content [80] also appear to level off in the third decade of life. Disc degeneration is virtually non-existent in young individuals and, starting in the third decade of life, increases with age [81]. Furthermore, students in their early twenties have smaller IVD height than people aged 40–45 years [84], indicating that some development still takes place between these ages. Also, a recent review [85] commented that the amount of aggrecan in the IVD levels off when individuals are in their early twenties.

Overall, like all organ systems in the human body, IVDs appear to have a certain timeline of development. Also like other organ systems in the human body [86], there is probably a 'critical period' in which load and other factors have a greater impact on the development of the IVD. This period is likely to be before an individual reaches their late twenties.

9 What Measurement Approaches can be Used in Humans?

To facilitate study of the impact of exercise on the IVD, it is important to understand the best measurement approaches. Currently, the best measurement approach is using MRI; while the assessment of body stature and measurement of lumbar disc height via ultrasound [87] are possible, the information provided is inferior to MRI. Table 2 lists the commonly used MRI approaches and describes their benefits and limitations.

In clinically oriented studies, mid-sagittal T2-weighted images are used and the IVDs are graded by a radiologist according to one of the many grading schemes present in the literature. Such grading schemes have often been used in studies of IVD degeneration (Table 1). However, such grading schemes have limitations when monitoring changes in the IVD in longitudinal or interventional studies. Specifically, a number of anatomical and signal intensity changes need to occur before a change in grade will be ascertained: this means a lot of information on IVD change is missed. Subsequently, a larger number of subjects is required to detect differences that occur either over time or due to an intervention. Furthermore, changes in IVD degeneration grade occur very slowly [77]. More sensitive, quantitative methods are required and we present these in Table 2.

One of the main difficulties with MRI techniques is in being able to make a biological interpretation of the results. Each outcome variable will be affected by glycosaminoglycan content, water content, collagen content and integrity of the collagenous rings of the IVD, to name but a few aspects. Knowing exactly what change in the IVD is behind the change in the MRI is difficult. It is important to use the same scanner, but even then comparisons between and within subjects over time need to be done carefully.

Table 2 Magnetic resonance imaging approaches for the assessment of the intervertebral disc

Approach	Advantages	Disadvantages
Grading of disc degeneration on T2-weighted images [93]	Standard clinical imaging sequence	Insensitive outcome measure
	Rapid sequence	Radiologist required for grading
	Commonly used methodology	
IVD morphology on T2-weighted images [94]	Standard clinical imaging sequence	Information only on disc geometry
	Rapid sequence	
IVD signal intensity on T2-weighted imaging with adjustment of signal intensity of cerebrospinal fluid [84, 95]	Standard clinical imaging sequence	Ability to compare between and within subjects over time is improved using cerebrospinal fluid as a reference, but still has limitations
	Rapid sequence	
T2-relaxation time	Related to IVD biochemistry [96–98]	Slightly longer sequence (7–12 min, depending on scanner and settings)
	Most well-studied research imaging sequence	Not available on all (clinical) scanners
		Specialised skills required for obtaining full information from imaging
		Definitive statements on IVD biochemistry difficult (in test subjects)
Apparent diffusion coefficient	Approach measures the speed of water diffusion in a particular tissue [99]	Low-resolution images
		Not available on all (clinical) scanners, though the MR technician can usually adapt brain diffusion-weighted imaging sequences for the spine
	Relates to IVD biochemistry [100]	Specialised skills required
	May give insight into the transport of small solutes within the IVD	Definitive statements on IVD biochemistry difficult (in test subjects)
		Since both apparent diffusion coefficient and T2-relaxation time co-vary, e.g. with age [101], it is unclear if this sequence delivers additional information in human test subjects
T1rho time	Relates to IVD biochemistry [102]	Slightly longer sequence (7–12 min, depending on scanner and settings)
		Not available on all (clinical) scanners
		Specialised skills required for obtaining full information from imaging
		Definitive statements on IVD biochemistry difficult (in test subjects)
		Since both T1rho time and T2-relaxation time co-vary, e.g. with age [88], it is unclear if this sequence delivers additional information in human test subjects
(Charged) contrast agents and T1 relaxation time	Thought to provide indicator of proteoglycan content of disc [103, 104]	Difficulty in data interpretation [9]
		Overall measurement approach takes a number of hours to perform
		Risk of adverse reactions to contrast agent
		Specialised skills required

IVD intervertebral disc, *MR* magnetic resonance

Another important issue is that whilst a number of imaging techniques have been developed, all of which aim, or claim, to measure different aspects of the IVD, it is not clear which approaches truly deliver unique information. For example, IVD T1rho- and T2-time both appear to show a similar pattern of change with age [88]. Do all the sequences simply co-vary? We are not aware of any work that has compared each of the approaches in the same individuals to address this question. Is it really worth the time, effort and money to perform a number of different imaging approaches, or will one or two suffice to give us the bulk of information we might want? These kinds of

questions need to be addressed and researchers need to exercise caution in choosing MRI sequences that, given the limitations of MRI, enable them to address their research question and ideally enable biological interpretations. We suggest implementing standard T2-weighted imaging, T2-relaxation time measurements and, for good measure, one of the other less well-studied research sequences.

10 Next Steps Forward in Research

What are the gaps in our knowledge on exercise and the IVD? What are the most likely fruitful steps forward in research on exercise and the IVD? The majority of human research studies focus on 'poor IVD health' (e.g. IVD degeneration): i.e. what is bad for the IVD, rather than what is good for the IVD. Shifting away from this will in part require the use and development of IVD measurement procedures that move away from radiological grading schemes and towards more quantitative methods that will enable assessment of finer changes in the IVD on shorter time scales. The interaction between the IVD and other parts of the spine, such as the vertebral end-plate, needs to be better understood. Other regions of the human spine, such as the cervical and thoracic region, need investigation.

Studies in humans of the impact of exercise on the IVD are required. Human research on the impact of exercise or ergonomics, although difficult, is important. Some studies have put 'exercise' [78] or 'sport' [52] into one large basket without any finer differentiation. This needs to change: we need to understand better which kinds of activity have what impact on the IVD.

Human studies in specific sporting populations, such as those involving non-contact, non-impact activities with a lower risk of acute injury, e.g. running, cycling and swimming, may provide a useful first port of call. However, if researchers evaluate different sporting types, it is worth considering that the IVDs and spinal structures of elite athletes may have adapted to the loads applied, especially if loading was performed during the developmental years. This may be expressed, for example, in a larger transverse plane IVD area (to reduce overall strain in the IVD) or altered vertebral body geometry.

Moving into prospective training studies could be a further step, but at the current juncture we do not know how long an intervention needs to be performed, or at what intensity, to have a measureable effect on the human IVD. For the first training studies, it may just be a matter of trial and error. It could also be worthwhile considering larger-scale prospective interventions in the workplace, such as by reducing sitting time with standing desks or forms of moderate physical activity.

11 Conclusions

In the current review we have examined the literature on the impact of loading and exercise on the IVD. On the basis of this review, it is clear that loading can have an impact on the IVD. Depending on the type of loading, this effect can be positive or negative. The characteristics of loading that are probably beneficial for the IVD if performed regularly for longer durations are dynamic but not rapid or explosive; in line with the normal function of the IVD (i.e. axial loading); and of a magnitude up to approximately those seen in jogging. The characteristics of loading that are probably detrimental for the IVD are static or very rapid; extremes of range or torsional activities; and magnitudes that are too low (e.g. lying) or too high (lifting in flexion, explosive tasks).

Clinical imaging sequences can be used to measure the IVD shape and size for quantification of characteristics of the IVD in humans, but are limited in their ability to provide information on IVD tissue composition. Grading schemes suffer significant limitations in smaller sample and effect sizes as they are insensitive outcome measures. Research imaging sequences, such as the measurement of T2-relaxation time, can be implemented to provide more information on IVD composition and to compare responses between individuals.

For future research we need to understand better which kinds of activity have what impact on the IVD in humans. Cross-sectional studies on sport and the IVD have provided indications of sports that are detrimental to the IVD, but we need to understand what loading and exercise types might be beneficial for it. There is some evidence that running-based sports might be beneficial for the IVD, and this could be a good avenue for further investigation. Finally, prospective training studies will be an important medium- to long-term step in investigating positive adaptation of the IVD to exercise in humans.

Compliance with Ethical Standards

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